

ucMGP [9]. Moreover, another intervention trial with MK-7 supplementation also demonstrates the effect on arterial stiffness [10]. In line with our observations, the sub-study of the ASTRONOMER trial also indicated high dephosphorylated MGP concentrations independently associated with a higher risk of progression of aortic stenosis [11].

Conclusions and expert recommendations

- Vitamin K status was identified as an independent predictor of the individual course of arterial stiffening. In theory, it can also be used as a therapeutic target to slow-down vascular aging.
- dp-ucMGP was identified as a promising tool for risk prediction and personalization of cardiovascular prevention.
- In concordance with PPPM principles, we support the creation of new multiparameter algorithms and multivariate models for risk assessment and patient stratification.

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Relevance of Lp-PLA₂ blood concentration for morphological structure of atherosclerotic plaque: a shift from reactive to predictive, preventive and personalized medicine to predict stroke in patients with asymptomatic internal carotid artery stenosis

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Background

Over one million Europeans are stroke-diagnosed annually [1]. Manifested atherosclerotic lesions of the carotid arteries account for approximately 40% of all ischemic strokes, and genetic predisposition, hypertension, among others are considered the best acknowledged risk factors [2]. However, the etiology of many stroke cases remains unclear, particularly in young patients below 50 years of age [2]. To this end, one of the most promising research areas involves the risks linked to the vascular inflammation and the follow-up cascade of pathological changes which altogether may lead to the clinical manifestation of stroke [3].

According to the EPMA criteria, clinically relevant biomarker-sets should serve for predictive diagnosis, targeted prevention and personalization of medical services, in order to contribute to the paradigm shift from reactive to 3PM [4]. Contextually, consideration of multi-factorial risks and individualized patient profiling provide comprehensive information for the clinically relevant biomarker-sets and multi-parametric analysis as tools for the 3PM implementation. A prospective pilot research project was carried out at the Clinic of Vascular Surgery of the Eastern Slovak Institute of Cardiovascular Diseases and the Faculty of Medicine of Pavol Jozef Safarik University, Kosice. The main criteria evaluated in our study included the degree of ICA stenosis, the morphological structure of the atherosclerotic plaque and the level of lipoprotein-associated phospholipase A₂ (Lp-PLA₂) concentration.

Working hypothesis

This project tested the hypothesis that the risk of stroke in patients with internal carotid artery (ICA) stenosis cannot be evaluated based on the determination of the degree of ICA stenosis only. In addition to stenosis, the morphological structure of the atherosclerotic plaque can serve as an important risk factor as well, while ulceration and instability of atherosclerotic plaques can be characterized by biomarkers.

Materials and methods

The study included 70 (27 females and 43 males) patients, who were hospitalized for carotid endarterectomy. The patients were divided into two groups depending on their symptoms: Group I included 30 patients with symptomatic ICA stenosis >50%; Group II comprised 70 patients with asymptomatic ICA stenosis >70%. There was no statistically significant difference in age and sex between the groups. Ultrasound scans were used to assess ICA stenosis, as well as the structure of the atherosclerotic plaque. Before surgery, blood samples were taken to determine the levels of the following biomarkers: Lp-PLA₂, IL-4, hemopexin, and homocysteine.

Results

When assessing the morphological structure of the atherosclerotic plaque using ultrasound, soft and mixed atherosclerotic plaques were detected in 73% of the patients in group I and 55% of the patients in group II. The comparison of Lp-PLA₂ concentration ratio revealed a statistically significant correlation ($p < 0.001$) between the increase in Lp-PLA₂ concentration in the patients with symptomatic ICA stenosis ($285.30 \pm 2.05 \mu\text{g/l}$) compared to the patients with asymptomatic ICA stenosis ($274.35 \pm 3.38 \mu\text{g/l}$). In 15% of asymptomatic patients with soft atherosclerotic plaque, Lp-PLA₂ level was higher ($293.90 \pm 1.5 \mu\text{g/l}$) than that in symptomatic patients with hard atherosclerotic plaque ($261.40 \pm 1.3 \mu\text{g/l}$). The concentration of Lp-PLA₂ correlated with atherosclerotic plaque structure rather than its size.

The comparison of serum hemopexin levels in symptomatic ($0.38 \pm 0.01 \text{ ng/l}$) and asymptomatic ($0.351 \pm 0.012 \text{ ng/l}$) patients revealed no statistically significant difference between both groups. In the patients with symptomatic ICA stenosis, the serum concentration of IL-4 ($65.77 \pm 3.78 \text{ ng/l}$) was found to be significantly higher compared to the patients with asymptomatic ICA stenosis ($42.69 \pm 1.73 \text{ ng/l}$).

The analysis of the homocysteine test revealed a statistically significant difference between the patients with symptomatic ICA stenosis and those with asymptomatic ICA stenosis. At the same time, homocysteine as a marker of atherosclerotic complications was inferior to Lp-PLA₂ when comparing the following risk factors, namely the degree of ICA stenosis, the morphological structure of the atherosclerotic plaque, and the concentration of the “optimal” marker.

Data interpretation

There is a wide range of vascular biomarkers; however, each biomarker has its own specificity and changes in its concentration may depend on different factors [3]. Among vascular markers analyzed, a statistically significant correlation between the degree of ICA stenosis, the structure of the atherosclerotic plaque and the clinical course were observed only in the case of Lp-PLA₂. The dominant factor for the increase in Lp-PLA₂ was the structure of the atherosclerotic plaque. According to the results of our study, unstable atherosclerotic plaques are typical for symptomatic patients, as well as for the patients with asymptomatic ICA stenosis. Our results are consistent with the results obtained by other authors who observed the patients with asymptomatic carotid stenosis and found that the patients with unstable echolucent plaques were 2.31 times more likely to develop stroke compared to the patients with stable plaque based on ultrasound findings [5]. Consideration of Lp-PLA₂ concentration in the patients with ICA stenosis may serve as an auxiliary criterion at the stage of determining and selecting treatment tactics for patients with ICA stenosis greater than 70%, and finally to apply a predictive and prognostic patient-specific treatment of atherosclerosis promoting the change from reactive medicine to 3PM. In addition, the proposed vascular biomarker Lp-PLA₂, which depends on the individual lipid profile, can be applied alternatively to the typical post-symptomatic treatment of atherosclerosis. HDL-associated Lp-PLA₂ may substantially contribute to the HDL antiatherogenic activity and could be additionally used to predict the efficacy of medication prescribed.

Conclusions

Our research demonstrated a statistically significant correlation between Lp-PLA₂ and the degree of ICA stenosis, the structure of the atherosclerotic plaque, and the clinical course. The increase in Lp-PLA₂ level (285.30 ng/ml ± 2.05) and ultrasound findings of soft atherosclerotic plaque in combination with stenosis degree may indicate a high embolic potential in the patients with ICA stenosis. Consideration of the morphological structure of the atherosclerotic plaque and Lp-PLA₂ concentration in the patients with ICA stenosis is recommended for the implementation of a personalized approach to therapies that meet the criteria of 3PM. The implementation of the 3PM strategy and personalized approach is one of the optimal directions to find the additional criteria for early identification of risk factors for stroke. It is anticipated that, ultimately, this change in diagnosis and therapy will help in the future design and development of new, more selective, and effective therapies for each individual patient.

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Contrast-enhanced ultrasound in detection of the endoleak: a possible role in a personalized approach to the follow-up after endovascular repair of the abdominal aneurysm

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